REMARKS

Status of the Claims

Claims 1, 5-8, 10 and 15-18 have been canceled without prejudice or disclaimer. Applicants reserve the right to seek allowance of these claims via continuing applications.

Claim 19 has been amended to recite "after discontinuation of antiviral drug therapy for Human Immunodeficiency Virus". Support for this amendment can be found, for example, on page 10, lines 17-27. Claim 20 has been amended to clarify that the subject has undetectable viral RNA levels upon discontinuation of antiviral drug therapy, in accordance with applicant's originally intended meaning. This amendment to claim 20 has not been made in view of any prior art or in response to a rejection by the Examiner. No new matter has been added by this amendment.

Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 19-26 stand rejected as not enabled by the specification. The Examiner states:

1) that the disclosure fails to demonstrate that low-dose IL-2 administration is effective at generating useful immune responses in patients who have measurable viral loads

2) that the disclosure fails to demonstrate that low-dose IL-2 administration is capable of generating the type of immune responses currently claimed

3) the prior art teaches that the administration of low-dose cytokines is unpredictable and often fails to have any meaningful clinical, immunological, or antiviral effects

4) the claims are directed to any virus, dose, and treatment, and

5) that the disclosure fails to provide a sufficient number of working embodiments.

Initially, applicant notes that, to advance prosecution, the claims now relate to administration of IL-2 after the discontinuation of antiviral therapy for HIV. While applicant respectfully disagrees with the Examiner's position, **point 4 above is rendered moot** in view of the newly submitted claim set.

Regarding **point 1** above, the Examiner states that:

> It is well documented that HIV-1 produces large quantities of virus. Thus, it is not readily manifest that low-dose IL-2 administration would display any meaningful effects in patients who have measurable viral loads. This is not surprising, since most patients generate robust immune responses that fail to control the virus.

Applicants respectfully submit that the Examiner's focus on viral loads is misplaced. The claims recite a method of *enhancing* the ability of the *immune system* to mount an effective immune response. Enhancing the immune system to mount an effective response does not require complete suppression of the viral load. Instead, immune enhancement is defined in the specification by maintaining a normal concentration of circulating CD4+ T cells with elevated CD8 + T cells and elevated Natural Killer cells (see page 15, lines 14-16). This language is recited in claim 19. Therefore enablement must be evaluated in view of maintaining a normal concentration of circulating CD4+ T cells with elevated CD8 + T cells and elevated Natural Killer cells beyond the normal range. See MPEP § 2164.08 ("All questions of enablement are evaluated against the claimed subject matter.")

Additional, direct evidence of *enhancing* the ability of the *immune system* to mount an effective immune response is submitted herewith. Applicant submits a Declaration showing CD 4+, CD 8+, and Natural Killer cell concentrations obtained from patients who have discontinued

antiviral therapy for HIV. Figure 1 shows that the CD 4+ T cell concentrations for a group of subjects who received IL-2 is maintained after discontinuation of antiviral therapy, as compared to baseline CD 4+ cell concentrations measured before antiviral therapy was discontinued. Figures 2 and 3 demonstrate that CD 8+ T cell and Natural Killer cell concentrations are elevated in patients receiving IL-2, again as compared to baseline cell concentrations before discontinuation of antiviral therapy. This data demonstrates that immune enhancement, as defined in the specification and recited in claim 19, is achieved when patients are administered IL-2 in accordance with the present invention.

Immune enhancement, as defined in the specification and recited in the claims, is achieved for patients who have discontinued antiviral therapy and have detectable levels of HIV. Comparing the cell concentrations of CD 4+, CD 8+, and Natural Killer Cells in Figures 1-3, and the viral loads shown in Figure 4, it is evident that these cell concentrations are *not* dependent on the HIV viral loads for those patients receiving low-dose IL-2. As set forth in the declaration, the data submitted with the declarations shows that CD 4+, CD 8+, and Natural Killer cell concentrations were not affected by the detectable HIV viral loads shown by patients after discontinuation of antiviral therapy, when these patients are administered low-dose IL-2. While the viral loads of patients receiving IL-2 in the attached declaration were initially below the lower limit of detection upon discontinuation of treatment, the Examiner has not provided any information that refutes the direct showing submitted herewith that immune enhancement, as defined in the claims, is not dependent on HIV viral loads.

Regarding **points 2 and 3 above**, applicant respectfully submits that the attached declaration, along with Example 2 of the specification show that low-dose IL-2 is capable of generating the type of immune response claimed. Figure 1 demonstrates that CD4 + T cell concentrations for the patients administered IL-2 were generally at or above baseline after discontinuation of antiviral therapy. Figure 2 demonstrates that CD8 + T cell concentrations for the IL-2 group were generally above baseline after discontinuation of antiviral therapy. Figure 3 demonstrates that Natural Killer cell concentrations for the IL-2 group were generally above baseline after discontinuation of antiviral therapy.

Regarding **point 5** above, applicant notes that the absence of working examples will not by itself render the invention non-enabled. MPEP § 2164.02 "None or One Working Example". Particularly:

> The presence of only one working example should never be the sole reason for rejecting the claims as being broader than the enabling disclosure, even though it is a factor to be considered along with all the other factors. Id.

Applicant submits that, upon consideration of all the factors discussed above, including the attached declaration, the claims are enabled and the rejection should be withdrawn.

In view of the above remarks, applicant believes the pending application is in condition for allowance.

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Respectfully submitted,

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Attachments